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Achroma Virus: A Gateway to Explore Virology Concepts

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Introduction

The Achroma virus is a virtual virus invented as a part of the virtual virus project in BIOL 450/Virology during the Fall of 2018. Viruses are tiny, abundant, and diverse packets of genetic material enclosed in a protein capsid. Viruses can infect many different types of life, from plants and animals to bacteria. In order to propagate, viruses need to infect a host cell, and hijack a living cell's machinery to build more of themselves. Some viruses destroy the host cell in order to release the newly synthesized viruses, a process known as lysis. Lysis is particularly damaging when the target cell of a virus is a cell type that cannot be regenerated after being lysed. A newly described virus, the Achroma virus, targets the photoreceptor cells specific to color vision, also known as the cones, of the human retina. Photoreceptor cells do not divide, which means that any colorblindness caused by viral damage to these cells is permanent (2,4).

The first notable appearance of the Achroma virus was at an elementary school in the United States. The school nurse noticed an unusually high number of children showing signs of colorblindness during standard annual vision testing. The nurse decided to re-test some of the children three weeks later and noticed that some of the children who hadn't appeared colorblind initially were beginning to show symptoms with time. She was concerned because colorblindness is normally a genetically linked trait and not something that develops over a period of a few weeks and spreads among a population. Upon investigation by additional medical professionals and specialists, it appeared that these students were losing color vision due to the destruction of the cone cells of their retinas. Intraocular fluid was taken from the eyes of several of the patients. DNA was isolated from this fluid and sequenced, which led to the discovery of the Achroma virus.

The goal of this report is to compile all the current information pertaining to Achroma virus, including the structure of the virus, its life cycle, its tools to trick the immune system, its pathology, and possible treatments.

Results and Discussion

1. Viral Structure

The Achroma virus is a naked, icosahedral virus.

It is on average 90 nm in diameter. It has twelve viral ligands: one on each vertex. These viral ligands are known as ROY ligands and they interact with the GBIV receptors on the surface of photoreceptor cells. These names were taken from ROY G. BIV, which is an acronym for the colors of the rainbow (red, orange, yellow, green, blue, indigo, violet). The viral capsid is composed of a repeating pattern of two distinct units. It houses linear, non-segmented, double-stranded DNA.

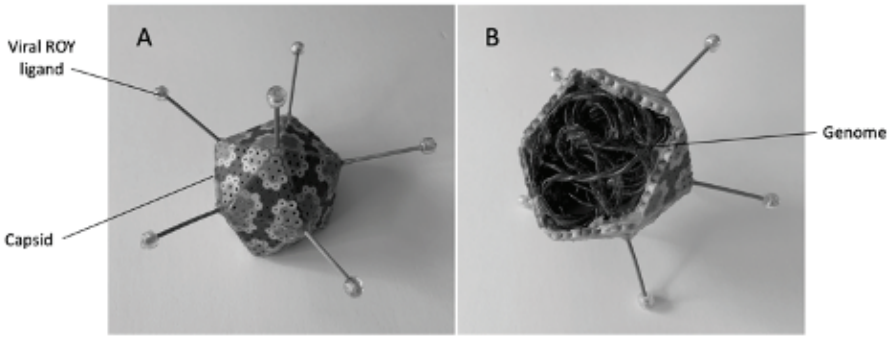

Figure 1. The structure of the Achroma virus. A – Outside view showing the icosahedral shape of the capsid as well as the repeating pattern. B – Inside view showing the viral genome inside the capsid. The ROY ligands can be seen in both images. The capsid of this model was made using plastic, fusible beads. The viral genome was made of plastic cord.

2. Life cycle

The entire virus enters the cell via receptor-mediated endocytosis (Fig. 2A). The virus attaches to the host photoreceptor cell when the viral ROY ligand binds to the GBIV receptor on the host cell surface. It is then endocytosed into the cell. Uncoating, or the degradation of the viral capsid, takes place in the endosome and the cytoplasm. Once the dsDNA is free of the capsid, it enters the nucleus via a nuclear pore (Fig. 2B).

Viral genome replication takes place in the nucleus. The viral genome encodes its own DNA polymerase, which is the enzyme that replicates the DNA. Photoreceptor cells are not actively dividing, so they are not duplicating their genome and using their own DNA polymerase. Therefore, it is more efficient for the virus to encode its own DNA polymerase and use the cellular protein manufacturing machinery to produce DNA. Also, the viral DNA polymerase includes a proofreading function, which helps to prevent mutations.

The virus relies on the photoreceptor cells' RNA polymerase for transcription of its mRNAs. RNA polymerase is the enzyme that "reads" the genes on

DNA and transcribes them into a form (mRNA) that the cell can ultimately use to make protein. In order to attract the cellular transcription machinery, the virus has evolved sequences on its genome that mimic the cellular promoters that normally attract the machinery to the cellular DNA. The viral genome also codes for a CAP-snatching enzyme that steals 5' CAPs from cellular mRNA and transfers them to viral mRNA. Because a 5' CAP is a necessary starting place for the cellular translation machinery when translating mRNA into proteins, the action of this CAP-snatching enzyme simultaneously makes the viral mRNA more competitive and puts the cellular mRNA at a disadvantage. The virus also relies on cellular poly-A polymerase to synthesize the mRNA's poly-A tails, which are another necessary component of mRNA for protein synthesis to occur. Any proteins synthesized by the cell's ribosomes that will be part of the viral capsid or viral ligands will move back into the nucleus for assembly. Once the capsids are assembled, the viral genomes enter the capsids thus completing the assembly of the viral particle (Fig. 2C).

When enough of the newly synthesized viruses accumulate in the cell, the pressure builds up and the new viruses break the cell membrane. The cell is lysed, and the new viruses are released to infect another cell (Fig. 2D).

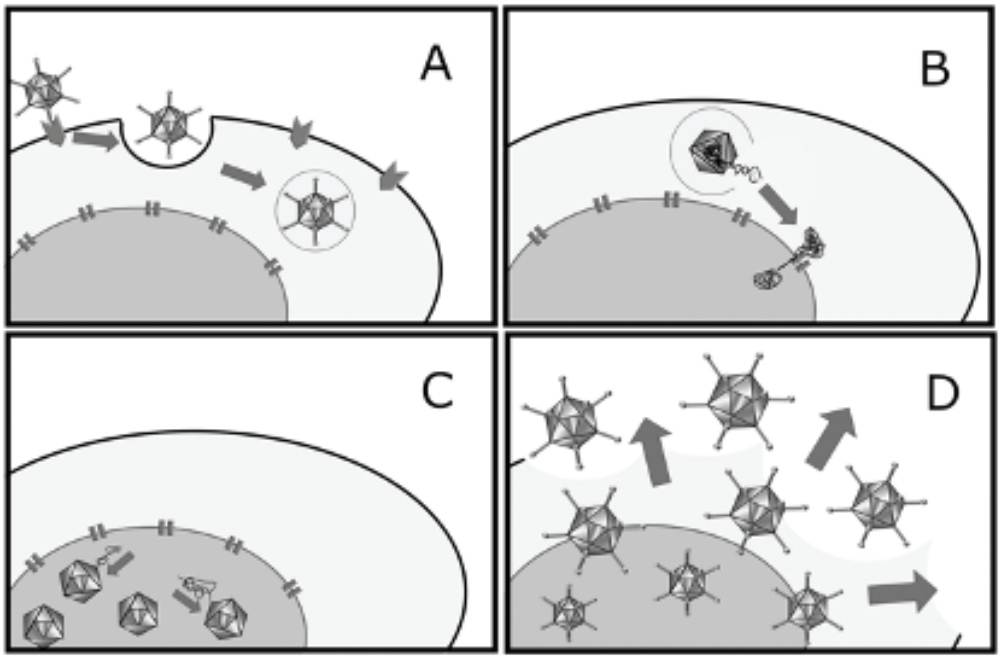

Figure 2. The life cycle of the Achroma virus. A - The virus enters the cell via receptor-mediated endocytosis. B - The viral capsid degrades in the endosome and cytoplasm. The dsDNA moves into the nucleus. DNA replication and transcription take place in the nucleus. Translation occurs in the cytoplasm when viral mRNA leaves the nucleus and is translated by a ribosome. C - Viral structural proteins move back into the nucleus and are assembled there. The viral genome is packaged in the empty capsids. D - The new viruses cause lysis of the cell.

This figure was prepared using Microsoft Powerpoint.

3. Immune system tricks

The immune system and viruses are in a continual evolutionary tug of war; viruses are constantly evolving ways to thwart the immune system and vice versa. The Achroma virus infects and lyses photoreceptor cells, which are located on the retina in the eye. The eye is one of the parts of the body that has immune privileged status. This means that the body has a limited immune response in this region. For example, a nonspecific immune response like inflammation is limited in the eye because inflammation would damage the delicate tissues there. The Achroma virus is able to establish itself in the eye without having to overcome some of the body's usual immune responses (1).

The Achroma virus also comes packaged with a specific protease, which is an enzyme that is responsible for cleaving or cutting a protein. This protease targets both MHC I and MHC II (Major Histocompatibility Complex I and II), which are key molecules on the surface of cells that help trigger an immune response. By damaging these proteins, the virus not only impedes the photoreceptor cells' ability to signal an immune response, but it also impedes the microglial cells' ability to signal one too. Microglial cells are immune macrophages found in the eye, and they cannot do their job and trigger an immune response without MHC II.

4. Pathology

The virus enters the patient through the eye. Because it does not have an envelope, it can live on surfaces for up to a day. It can be easily transmitted by touching a contaminated surface and then rubbing the eyes. Symptoms of Achroma virus infection can mimic those of conjunctivitis or other eye infections, including watery eyes, discharge from eyes, and redness. The virus can be present in these fluids, and if they get on the patient's hands the patient can then contaminate surfaces, thus facilitating the transfer of the virus to other individuals.

The Achroma virus targets the photoreceptor cells of the retina, which means that eventually it degrades the patient's vision. Usually, the patient notices color vision declining first, because there are fewer cones than rods in the retina. Also, cones and rods are spatially separated, so the new virus can easily access many cones in one area. The patient also may notice eye "floaters" or other disturbances in vision. Rarely the Achroma infection has been observed to progress to complete blindness if the virus was left untreated. It is suspected that persistent inflammation triggered by large amounts of Achroma virus might be inflicting

extensive damage to rod cells and thus loss of vision (3). It is not known if other factors, for example, genetic variation or environmental exposures, contribute to this unfortunate outcome.

5. Treatment and Therapeutic Use

Antiviral drugs are currently being developed to treat Achroma virus infections. The tests involve a drug that targets the viral MHC protease. The drug is injected directly into the posterior chamber of the affected eye to try and achieve the fastest effect. The best methods to prevent an Achroma virus infection are frequent hand washing and making sure contact lenses are kept in a clean and sanitary environment.

Since the Achroma virus can readily enter photoreceptor cells, there is research being done on using empty Achroma virus capsids to offer gene therapy to colorblind patients. Functional copies of genes for photopigments may be able to be packaged in the capsids and sent into photoreceptor cells. This research is still very new and further studies will need to be done to confirm the efficacy and safety of such techniques.

6. Impact on the Author

The creation of the Achroma virus through the virtual virus project has influenced how I will think about teaching science in my classroom in the future. Even though the material in this course was well above elementary level, I believe I can apply the principles of this project to my own elementary school classroom someday. This project was an engaging means of modelling the scientific process in a condensed but realistic way. It also required us to integrate both newly acquired knowledge and existing knowledge over the course of the semester. Applying the material in a meaningful way is more effective than just memorization. I think the creative aspect of this project enhances learning, because students are more excited and motivated to make the subject matter their own.

Acknowledgements

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References

Forrester JV, Heping X. *Good news-bad news: the Yin and Yang of immune privilege in the eye*. Frontiers in Immunology. 3: 338.

Herrero Uribe L. *Viruses, definitions and reality.* Revista de Biología Tropical. 59 (3): 993-998.

Purves D, Augustine GJ, Fitzpatrick D, et al. *Anatomical Distribution of Rods and Cones*. Neuroscience. 2nd edition. Sinaeur Associates; 2001.

Shors T. Understanding Viruses. 3rd edition. Jones and Bartlett Learning. 2017.

About the Author

Allyssa Richardson is graduating in Spring 2020 as an Elementary Education and Biology double major. Her project was completed for BIOL450/Virology under the mentorship of Dr. Boriana Marintcheva (Biological Sciences). In the future, Alyssa plans to pursue graduate studies at Bridgewater State University and eventually become a teacher at an elementary school.